Minutes
Hirschsprung Disease Research Collaborative (HDRC) Conference Call
October 16, 2017, 2:30pm EST

Attendees:
Aravinda Chakravarti, Dallas Auer, Juli Bollinger, Courtney Berrios, and Jia Yan (Johns Hopkins University School of Medicine); Lois Sayrs (Phoenix Children's Hospital); Ling Fan (Nationwide Children's Hospital); Jill Ketzer (Children's Hospital Colorado); Lynda Painting (University of California, Davis); Raj Kapur (Seattle Children's Hospital); Michael Rollins (University of Utah Primary Children's Center); Hector Monforte (Johns Hopkins All Children's Hospital); Jack Langer (Hospital for Sick Children)

I. Welcome
   a. Dr. Chakravarti thanked everyone for joining the call and for their continuing efforts at recruitment of participants.

II. Membership and samples
   a. HDRC sites have continued to enroll families for the biorepository over the past quarter. During the period from April 28, 2017 to October 16, 2017 the following have been enrolled: All Children's Hospital - 2 families, Valley Children's - 1 family, Emory University – 1 family, Nationwide Children's Hospital – 3 families, Penn State Hershey Children's Hospital – 4 families, Seattle Children's Hospital – 6 families, Texas Children's Hospital – 3 families, University of Utah Primary Children's Hospital – 6 families.
   b. HDRC membership update: Jill Ketzer has been working on the IRB application for the HDRC's newest site, the Children's Hospital Colorado, and the application is close to being submitted.

III. Recruitment
   a. The current enrollment count consists of 440 probands and 637 of their family members, for a total of 1,077 participants who are enrolled in the HDRC as of October 16, 2017. Our deepest gratitude to everyone for all of their efforts in enrolling participants for the HDRC.
   b. The following is a summary of recruitment by type of relative:

Membership Summary Table

Category	Total
Proband	440
Father	246
Mother	360
Sibling	21
Other relative	10
Total	1077

   c. As shown above, recruitment includes multiple first-degree relatives, but does not always include the entire nuclear family. Our goal is, of course, to obtain the full family whenever possible. Jia discussed the causes of this difficulty and possible solutions. One of the reported impediments is that families do not often go to the clinic visit together; for example, a parent often stays home with the other sibling(s). Jack Langer agreed with this scenario and also suggested that parents in some families may have separated, making it difficult to recruit both parents. Dr. Chakravarti said that whether both parents are available may depend on time of recruitment, as many families enroll shortly after the birth of their child. Raj Kapur suggested that perhaps it would be helpful to have other recruitment options for samples, such as blood spot/card at home.

d. Dr. Langer asked how many trios we currently have in the HDRC. On checking our records following this meeting, we have identified 220 independent trios with DNA.
e. It may be helpful to assess the percentage of families for which only one parent enrolled and assessing whether each center can target the other parent for recruitment. Jia Yan has created a list of families with complete and incomplete trios and will follow up with each site to assess whether it would be possible to complete these families.

IV. Update on development of the REDCap database
a. Ray Everngam from the Hendren Project has been developing the data dictionary based on the data structure of the local Hirschsprung disease study at Johns Hopkins, which will then be used as the basis for the REDCap database for the HDRC.
b. The REDCap database may help with recruitment and completion of questionnaires by allowing for completion via an online link at home or at a kiosk at the clinic.
c. Feedback from all HDRC members is welcome for the development of the HDRC database. It would be helpful to have volunteers for the testing phase of the database development to input data and provide feedback for completion of the questionnaire.
d. Dr. Langer suggested that it would be beneficial to gather additional clinical information over time. REDCap is well-suited for longitudinal data, and this will be an important future aim for the HDRC pending funding.

V. Summary of HDRC data
a. Please see below for a table summarizing characteristics of participants for whom we currently have clinical data in the HDRC vs. participants in the local Genetic Analysis of Hirschsprung Disease study (HSCR) at Johns Hopkins University.

	HSCR (n = 633, 498 families)		**HDRC (n = 407, 301 families)**	
Individual/Family Characteristic	**N**	**(%)**	**N**	**(%)**
Sex				
Male	425	(67.14)	299	(73.50)
Female	208	(32.90)	108	(26.50)
Segment Length				
Short segment	249	(57.24)	193	(76.28)
Long segment	74	(17.01)	21	(8.30)
Total colonic aganglionosis	112	(25.75)	39	(15.42)
Family Type				
Simplex	349	(70.08)	249	(82.70)
Multiplex	149	(29.92)	52	(17.30)
Family Phenotypic Class				
Isolated HSCR	306	(62.70)	189	(65.40)
Known syndrome	55	(11.24)	31	(10.73)
Down syndrome	41	(8.30)	25	(8.65)
Other chromosomal anomaly	9	(1.84)	3	(1.04)
Single gene disorder	3	(0.61)	3	(1.04)
Additional anomalies	129	(27.29)	69	(23.88)

b. The HDRC has collected families with rates of additional anomalies that are comparable to those of the local genetic study at Johns Hopkins.
c. There are currently 106 families that are missing data from questionnaires. Data table will continue to be updated as data becomes more complete for these families.

d. Jack Langer suggested that there may still be some bias in ascertainment for the HDRC, as many of the cases he sees are more severe cases. Raj Kapur reported that Seattle Children's Hospital receives referrals for more complicated cases from the community-based hospital. Many HDRC site are large academic hospitals. Dr. Chakravarti suggested that it would be helpful to compare data across sites to better understand ascertainment biases.
e. Dallas Auer analyzed the HDRC samples and created a sample summary document, which has been circulated to the HDRC. Dr. Chakravarti suggested that it may be helpful to provide a sample summary for each individual HDRC site as we gather more data.

VI. Grant application for the HDRC
a. Dr. Chakravarti has made a request to the NIDDK to apply for an R01 that exceeds $500,000 per year, and up to $1,000,000, in funding.
b. The next February 5th R01 deadline will be after the implementation date of January 25, 2017 for the requirement of a single IRB (sIRB) for all multi-site research studies funded by the NIH. The grant will need to include plans for moving to an sIRB, and the HDRC will eventually move to an sIRB if it receives NIH funding. Additional details of the move will be part of future discussions.
c. NCATS has developed a SMART IRB Reliance agreement (https://smartirb.org/) to facilitate setting up an sIRB. This tool eliminates the need for study-specific reliance agreement negotiations. Once an institution is a signatory to the SMART IRB reliance agreement, it can use SMART as the reliance agreement for any specific study that also involves institutions that are SMART signatories.
d. Most HDRC sites in the US are already part of SMART IRB. The attached HDRC member table includes a column indicating which institutions have already signed onto SMART IRB.
e. The new policy does not apply to sites that are international.

VII. The next HDRC Quarterly Call will be scheduled for January 31, 2018 from 1:00pm – 2:00pm Eastern Standard Time.
a. Call-in information:
    i. CALL IN NUMBER: 515-604-9304
    ii. ACCESS CODE: 172048#